

PCT

## REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference  
(if desired) (12 characters maximum)

P6824WO CTH

## Box No. I TITLE OF INVENTION

Cell Line

## Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

University College London  
Brook House  
2-16 Torrington Place  
London  
WC1E 7HN  
United Kingdom

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State (i.e. country) of nationality:

United Kingdom

State (i.e. country) of residence:

United Kingdom

This person is applicant for the purposes of:

☐ all designated States☒ all designated States except the United States of America☐ the United States of America only☐ the States indicated in the Supplemental Box

## Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

University of Newcastle  
Newcastle Upon Tyne  
NE1 7RU  
United Kingdom

This person is:

☒ applicant only☐ applicant and inventor☐ inventor only (if this check-box is marked, do not fill in below)

State (i.e. country) of nationality:

United Kingdom

State (i.e. country) of residence:

United Kingdom

This person is applicant for the purposes of:

☐ all designated States☒ all designated States except the United States of America☐ the United States of America only☐ the States indicated in the Supplemental Box☒ Further applicants and/or (further) inventors are indicated on a continuation sheet

## Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

☒ agent☐ common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

HARDING, Charles Thomas  
D Young & Co  
21 New Fetter Lane  
London  
EC4A 1DA  
United Kingdom

Telephone No.

+ 23 8063 4816

Facsimile No.

+ 23 8022 4262

Teleprinter No.

477667 YOUNGS G

☐ Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

## Continuation of Box No. III FURTHER APPLICANT (S) AND/OR (FURTHER) INVENTOR(S)

*If none of the following sub-boxes is used, this sheet is not to be included in the request.*

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

YEAMAN, Steve  
School of Biochemistry and Genetics  
University of Newcastle  
Framlington Place  
Newcastle-Upon-Tyne  
NE2 4HH  
United Kingdom

This person is:

- ☐ applicant only  
☒ applicant and inventor  
☐ inventor only (if this check-box is marked, do not fill in below)

State (that is, country) of nationality:

British

State (that is, country) of residence:

United Kingdom

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

SHEPHERD, Peter  
Department of Biochemistry  
University College London  
Gower Street  
London, WC1E 6BT  
United Kingdom

This person is:

- ☐ applicant only  
☒ applicant and inventor  
☐ inventor only (if this check-box is marked, do not fill in below)

State (that is, country) of nationality:

New Zealand

State (that is, country) of residence:

United Kingdom

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

ZORZANO, Antonio  
Dept de Bioquímica i Fisiològica  
Facultat de Biologia  
Universitat de Barcelona  
Avinguda Diagonal 645  
08028 Barcelona  
Spain

This person is:

- ☐ applicant only  
☒ applicant and inventor  
☐ inventor only (if this check-box is marked, do not fill in below)

State (that is, country) of nationality:

Spanish

State (that is, country) of residence:

Spain

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only  
☐ applicant and inventor  
☐ inventor only (if this check-box is marked, do not fill in below)

State (that is, country) of nationality:

State (that is, country) of residence:

This person is applicant for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on a continuation sheet

**Supplemental Box***If the Supplemental Box is not used, this sheet need not be included in the request.***Use this box in the following cases:****1. If, in any of the Boxes, the space is insufficient to furnish all the information:***in particular:*

- (i) if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available:
- (ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked:
- (iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America:
- (iv) if, in addition to the agent(s) indicated in Box No. IV, there are further agents:
- (v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "Continuation" or "Continuation-in-part":
- (vi) if there are more than three earlier applications whose priority is claimed:

*in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient;*

*in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below;*

*in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;*

*in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;*

*in such case, write "Continuation of Box No. IV and indicate for each further agent the same type of information as required in Box No. IV;*

*in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;*

*in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI.*

**2. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty:**

*in such case, write "Statement Concerning Non-Prejudicial Disclosures or Exceptions to Lack of Novelty" and furnish that statement below.*

Continuation of Box No. IV  
 COTTER, Ivan John  
 PILCH, Adam John Michael  
 CRISP, David Norman  
 ROBINSON, Nigel Alexander Julian  
 HARRIS, Ian Richard  
 HARDING, Charles Thomas  
 TURNER, James Arthur  
 MALLALIEU, Catherine Louise  
 PRATT, Richard Wilson  
 PRICE, Paul Anthony King  
 HOLMES, Miles  
 HORNER, David Richard  
 MASCHIO, Antonio  
 NACHSHEN, Neil  
 POTTER, Julian  
 HAINES, Miles John  
 ALCOCK, David  
 MATHER, Belinda Jane  
 BODEN, Keith McMurray  
 DEVILE, Jonathan Mark

**Box No. V DESIGNATION OF STATES**

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

**Regional Patent**

- ☒ **AP** ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA** Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP** European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA** OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, please specify on dotted line)

**National Patent (if other kind of protection or treatment desired, specify on dotted line):**

- |   |   |
|---|---|
| <input checked="" type="checkbox"/> <b>AE</b> United Arab Emirates                  | <input checked="" type="checkbox"/> <b>LS</b> Lesotho                                   |
| <input checked="" type="checkbox"/> <b>AL</b> Albania                               | <input checked="" type="checkbox"/> <b>LT</b> Lithuania                                 |
| <input checked="" type="checkbox"/> <b>AM</b> Armenia                               | <input checked="" type="checkbox"/> <b>LU</b> Luxembourg                                |
| <input checked="" type="checkbox"/> <b>AT</b> Austria                               | <input checked="" type="checkbox"/> <b>LV</b> Latvia                                    |
| <input checked="" type="checkbox"/> <b>AU</b> Australia                             | <input checked="" type="checkbox"/> <b>MA</b> Morocco                                   |
| <input checked="" type="checkbox"/> <b>AZ</b> Azerbaijan                            | <input checked="" type="checkbox"/> <b>MD</b> Republic of Moldova                       |
| <input checked="" type="checkbox"/> <b>BA</b> Bosnia and Herzegovina                | <input checked="" type="checkbox"/> <b>MG</b> Madagascar                                |
| <input checked="" type="checkbox"/> <b>BB</b> Barbados                              | <input checked="" type="checkbox"/> <b>MK</b> The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> <b>BG</b> Bulgaria                              |   |
| <input checked="" type="checkbox"/> <b>BR</b> Brazil                                | <input checked="" type="checkbox"/> <b>MN</b> Mongolia                                  |
| <input checked="" type="checkbox"/> <b>BY</b> Belarus                               | <input checked="" type="checkbox"/> <b>MW</b> Malawi                                    |
| <input checked="" type="checkbox"/> <b>CA</b> Canada                                | <input checked="" type="checkbox"/> <b>MX</b> Mexico                                    |
| <input checked="" type="checkbox"/> <b>CH AND LI</b> Switzerland and Liechtenstein  | <input checked="" type="checkbox"/> <b>NO</b> Norway                                    |
| <input checked="" type="checkbox"/> <b>CN</b> China                                 | <input checked="" type="checkbox"/> <b>NZ</b> New Zealand                               |
| <input checked="" type="checkbox"/> <b>CR</b> Costa Rica                            | <input checked="" type="checkbox"/> <b>PL</b> Poland                                    |
| <input checked="" type="checkbox"/> <b>CU</b> Cuba                                  | <input checked="" type="checkbox"/> <b>PT</b> Portugal                                  |
| <input checked="" type="checkbox"/> <b>CZ</b> Czech Republic                        | <input checked="" type="checkbox"/> <b>RO</b> Romania                                   |
| <input checked="" type="checkbox"/> <b>DE</b> Germany                               | <input checked="" type="checkbox"/> <b>RU</b> Russian Federation                        |
| <input checked="" type="checkbox"/> <b>DK</b> Denmark                               | <input checked="" type="checkbox"/> <b>SD</b> Sudan                                     |
| <input checked="" type="checkbox"/> <b>DM</b> Dominica                              | <input checked="" type="checkbox"/> <b>SE</b> Sweden                                    |
| <input checked="" type="checkbox"/> <b>EE</b> Estonia                               | <input checked="" type="checkbox"/> <b>SG</b> Singapore                                 |
| <input checked="" type="checkbox"/> <b>ES</b> Spain                                 | <input checked="" type="checkbox"/> <b>SI</b> Slovenia                                  |
| <input checked="" type="checkbox"/> <b>FI</b> Finland                               | <input checked="" type="checkbox"/> <b>SK</b> Slovakia                                  |
| <input checked="" type="checkbox"/> <b>GB</b> United Kingdom                        | <input checked="" type="checkbox"/> <b>SL</b> Sierra Leone                              |
| <input checked="" type="checkbox"/> <b>GD</b> Grenada                               | <input checked="" type="checkbox"/> <b>TJ</b> Tajikistan                                |
| <input checked="" type="checkbox"/> <b>GE</b> Georgia                               | <input checked="" type="checkbox"/> <b>TM</b> Turkmenistan                              |
| <input checked="" type="checkbox"/> <b>GH</b> Ghana                                 | <input checked="" type="checkbox"/> <b>TR</b> Turkey                                    |
| <input checked="" type="checkbox"/> <b>GM</b> Gambia                                | <input checked="" type="checkbox"/> <b>TT</b> Trinidad and Tobago                       |
| <input checked="" type="checkbox"/> <b>HR</b> Croatia                               | <input checked="" type="checkbox"/> <b>TZ</b> United Republic of Tanzania               |
| <input checked="" type="checkbox"/> <b>HU</b> Hungary                               | <input checked="" type="checkbox"/> <b>UA</b> Ukraine                                   |
| <input checked="" type="checkbox"/> <b>ID</b> Indonesia                             | <input checked="" type="checkbox"/> <b>UG</b> Uganda                                    |
| <input checked="" type="checkbox"/> <b>IL</b> Israel                                | <input checked="" type="checkbox"/> <b>US</b> United States of America                  |
| <input checked="" type="checkbox"/> <b>IN</b> India                                 |   |
| <input checked="" type="checkbox"/> <b>IS</b> Iceland                               | <input checked="" type="checkbox"/> <b>UZ</b> Uzbekistan                                |
| <input checked="" type="checkbox"/> <b>JP</b> Japan                                 | <input checked="" type="checkbox"/> <b>VN</b> Viet Nam                                  |
| <input checked="" type="checkbox"/> <b>KE</b> Kenya                                 | <input checked="" type="checkbox"/> <b>YU</b> Yugoslavia                                |
| <input checked="" type="checkbox"/> <b>KG</b> Kyrgyzstan                            | <input checked="" type="checkbox"/> <b>ZA</b> South Africa                              |
| <input checked="" type="checkbox"/> <b>KP</b> Democratic People's Republic of Korea | <input checked="" type="checkbox"/> <b>ZW</b> Zimbabwe                                  |
| <input checked="" type="checkbox"/> <b>KR</b> Republic of Korea                     |   |
| <input checked="" type="checkbox"/> <b>KZ</b> Kazakhstan                            | <input checked="" type="checkbox"/> <b>DZ</b> Algeria                                   |
| <input checked="" type="checkbox"/> <b>LC</b> Saint Lucia                           | <input checked="" type="checkbox"/> <b>AG</b> Antigua and Barbuda                       |
| <input checked="" type="checkbox"/> <b>LK</b> Sri Lanka                             | <input checked="" type="checkbox"/> <b>MZ</b> Mozambique                                |
| <input checked="" type="checkbox"/> <b>LR</b> Liberia                               | <input checked="" type="checkbox"/> <b>BZ</b> Belize                                    |

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after the issuance of this sheet:

**Precautionary Designation Statement:** In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)

**Box No. VI PRIORITY CLAIM**☐

Further priority claims are indicated in the Supplemental Box

Filing Date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application: * regional Office	international application: receiving Office
item (1) 13 Jul 1999 13/7/1999	9916400.6	UK		
item (2)				
item (3)				

- ☒ The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): (1)

\* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

**Box No. VII INTERNATIONAL SEARCHING AUTHORITY**

**Choice of International Searching Authority (ISA)**  
(If two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA / EPO

**Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):**

Date (day/month/year)

Number:

Country (or regional Office):

**Box No. VII CHECK LIST; LANGUAGE OF FILING**

This international application contains the following number of sheets:

request : 5  
description (excluding  
sequence listing part) : 18  
claims : 2  
abstract : 1  
drawings : 0  
sequence listing part of  
description : 1  
Total number of  
sheets : 27

This international application is accompanied by the item(s) marked below:

- ☒ fee calculation sheet
- ☐ separate signed power of attorney
- ☐ copy of general power of attorney; reference number, if any:
- ☐ statement explaining lack of signature
- ☐ priority documents(s) identified in Box No. VI as item(s):
- ☐ translation of international application into (language):
- ☐ separate indications concerning deposited microorganism or other biological material
- ☐ nucleotide and/or amino acid sequence listing in computer readable form
- ☒ other (specify): Letter

Figure of the drawings which  
should accompany the abstract:

Language of filing of the  
international application:

English

**Box No. IX SIGNATURE OF APPLICANT OR AGENT**

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request)



HARDING, Charles Thomas

For receiving Office use only

1. Date of actual receipt of the purported international application:	2. Drawings:  <input type="checkbox"/> received:  <input type="checkbox"/> not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority specified (if two or more are competent): ISA /	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee paid

For International Bureau use only

Date of receipt of the record copy by  
the International Bureau:

From the INTERNATIONAL SEARCHING AUTHORITY

**PCT**NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

(PCT Rule 44.1)

To:

D. YOUNG & CO.  
Attn. HARDING, Charles Thomas  
21 New Fetter Lane  
London EC4A 1DA  
UNITED KINGDOM

SOUTHAMPTON

DS CTH  
DUE 27/01  
COMPUTER NO 140Date of mailing  
(day/month/year)

27/11/2000

Applicant's or agent's file reference

P6824W0 CTH

**FOR FURTHER ACTION**

See paragraphs 1 and 4 below

International application No.

PCT/GB 00/ 02674

International filing date  
(day/month/year)

11/07/2000

Applicant

UNIVERSITY COLLEGE LONDON

- 1.
- ☒
- The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Fascimile No.: (41-22) 740.14.35**For more detailed instructions,** see the notes on the accompanying sheet.

- 2.
- ☐
- The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

- 3.
- ☐
- With regard to the protest**
- against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

- 4.
- Further action(s):**
- The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority

 European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Jaap Hurenkamp

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.



## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>P6824WO CTH</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB 00/ 02674</b>	International filing date (day/month/year) <b>11/07/2000</b>	(Earliest) Priority Date (day/month/year) <b>13/07/1999</b>
Applicant <b>UNIVERSITY COLLEGE LONDON</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**METHOD TO STUDY INSULIN ACTION**

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/50 G01N33/74 C07K14/72 C12N5/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, CHEM ABS Data, BIOSIS, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 23231 A (MAX-PLANCK-GESELLSCHAFT ZUR FÖRDERUNG DER WISSENSCHAFTEN E.V.) 31 August 1995 (1995-08-31) page 1, line 8 - line 16; claim 9 page 4, line 33 -page 5, line 1 page 16, point 5.2 -----	1-9



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents :

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&amp;\* document member of the same patent family

Date of the actual completion of the international search

17 November 2000

Date of mailing of the international search report

27/11/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Van Bohemen, C

# INTERNATIONAL SEARCH REPORT

## Information on patent family members

PCT/GB 00/02674

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9523231 A	31-08-1995	AU 1812595 A US 5856111 A	11-09-1995 05-01-1999
-----			

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE  
 in its capacity as elected Office

Date of mailing (day/month/year) 23 May 2001 (23.05.01)	
International application No. PCT/GB00/02674	Applicant's or agent's file reference P6824WO CTH
International filing date (day/month/year) 11 July 2000 (11.07.00)	Priority date (day/month/year) 13 July 1999 (13.07.99)
Applicant YEAMAN, Steve et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
02 February 2001 (02.02.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Juan Cruz
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/02674

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9523231 A	31-08-1995	AU 1812595 A US 5856111 A	11-09-1995 05-01-1999

## PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTICE INFORMING THE APPLICANT OF THE  
COMMUNICATION OF THE INTERNATIONAL  
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

HARDING, Charles, Thomas  
D. Young & Co.  
21 New Fetter Lane  
London EC4A 1DA  
ROYAUME-UNI

NOTICE	
ORDER	
RECD - 9 APR 2001	
ANSO	
ENTRY	
FOR	

Date of mailing (day/month/year) 29 March 2001 (29.03.01)		IMPORTANT NOTICE	
Applicant's or agent's file reference P6824WO CTH			
International application No. PCT/GB00/02674	International filing date (day/month/year) 11 July 2000 (11.07.00)	Priority date (day/month/year) 13 July 1999 (13.07.99)	
Applicant UNIVERSITY COLLEGE LONDON et al			

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:  
AU,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:  
AE,AG,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,BZ,CA,CH,CN,CR,CU,CZ,DE,DK,DM,DZ,EA,EE,EP,ES,  
FI,GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,  
MN,MW,MX,MZ,NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU,  
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).
3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 29 March 2001 (29.03.01) under No. WO 01/22082

## REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

## REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer J. Zahra Telephone No. (41-22) 338.83.38
--	---

PCT

REC'D 08 OCT 2001

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P006824WO CTH	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/02674	International filing date (day/month/year) 11/07/2000	Priority date (day/month/year) 13/07/1999
International Patent Classification (IPC) or national classification and IPC C12Q1/00		
Applicant UNIVERSITY COLLEGE LONDON		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 8 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  02/02/2001	Date of completion of this report  02.10.2001
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Herrero, M  Telephone No. +49 89 2399 8542



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB00/02674

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-19 as originally filed

**Claims, No.:**

1-9 as originally filed

**Sequence listing part of the description, pages:**

1, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB00/02674

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims 2, 8
	No:	Claims 1, 3-7, 9
Inventive step (IS)	Yes:	Claims
	No:	Claims 1-9
Industrial applicability (IA)	Yes:	Claims 1-9
	No:	Claims

2. Citations and explanations  
**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:  
**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

## **SECTION V**

### **2. CITATIONS AND EXPLANATIONS**

2.1 The following documents have been considered for the purposes of this report:

D1: WO 95/23231

D2: Sarabia, V. et al (1990) Biochem. Cell. Biol. **68**:536-542

D3: Hurel, S.J. et al (1996) Biochem. J. **320**:871-877 (also cited in the application)

The documents D2 and D3 were not cited in the international search report. Copies of the documents have been provided to the Applicants.

### **2.2 Novelty and inventive step (Art. 33(2) and (3) PCT)**

The present application does not satisfy the criteria set forth in Article 33(2) and (3) PCT because,

- a) the subject-matter of Claims 1, 3, 4, 5, 6, 7 and 9 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT)
- b) the subject-matter claimed does not involve an inventive step (Rule 65(1)(2) PCT).

D1 describes stable co-transfected cell lines for the identification of substances affecting insulin receptor mediated signal transduction, in particular genetically engineered baby hamster kidney (BHK) cells co-expressing the insulin receptor (IR) and the receptor protein tyrosine phosphatase (RPTP $\alpha$  or RPTP $\epsilon$ ).

Taking into account the definitions of the generic terms "immortalized", "factor", "insulin action" and "affects insulin action" given in the present application (cf page 3, lines 1-23) those methods disclosed in D1 for screening, identification and evaluation of compounds that interact with RPTP $\alpha$ , RPTP $\epsilon$  and IR and may affect

various cellular processes under the control of the insulin signalling pathway, which rely on the use of the therein characterized stably transfected BHK cells (cf page 6, lines 4-18; page 12, lines 28-36 bridging over page 13, lines 1-15 and page 26, line 9-page 24, line 5) would appear to fall under the wording of the broadly formulated methods of studying insulin action in a cell line according to present Claims 1 and 6. The subject-matter of these claims is therefore neither novel nor inventive over D1 (Art. 33(2) and (3) PCT).

D2 analyses the glucose uptake process in human and animal muscle cells in culture. For this purpose D2 discloses the preparation of human muscle cell clones of primary origin. The regulation by insulin of glucose uptake in fused myotubes of human muscle cells in culture is compared with the corresponding response in cultures of muscle cell lines originated from rat (L6) and mouse (C2C12), either in the absence or in the presence of the inhibitor of glucose transport cytochalasin B (cf Figures 2, 3 and Table 1 on pages 538-540). D2 concludes that human muscle cell clones may be useful to study the regulation of hexose uptake in cells from human subjects with hereditary defects in carbohydrate metabolism and instrumental in the investigation of the mechanism of action of antidiabetic drugs that act at the level of glucose utilization (cf page 541, right column, end of the Discussion).

According to the present application (cf page 7, lines 4-6 and page 10, lines 17-18) both cell lines L6 and C2C12 referred to in D2 are immortalized muscle cell lines. Thus, as long as the origin of the "immortalized cell line" of interest is not identified in the present claims, the content of D2 destroys the novelty of Claims 1, 3, 4, 5 and 7.

Moreover, irrespective of its intended subsequent use, the cell line of unidentified origin claimed *per se* according to present Claim 9 appears to be neither novel nor inventive vis-à-vis the aforementioned cell lines disclosed in D1 (stably transfected BHK cell lines) and D2 (immortalized L6 and C2C12 cell lines).

D3, which discloses an approach for studying the insulin action in human muscle cells based on (i) the use of inhibitors and potentiators of insulin action or (ii) the modulation of key enzymes involved in the insulin signalling cascade, is regarded

as being the closest prior art document. As referred to in the present application, the methods carried out in D3 rely on the use of primary cultures of human myoblasts. D3 concludes that human myoblasts are an appropriate model system in which to study insulin signalling in human tissue and indicates the possibility of culturing cells from insulin-resistant subjects for identifying molecular mechanisms contributing to such resistance (page 876, right column, last paragraph of the discussion).

The technical problem to be solved by the present application essentially relates to the provision of an improved type of human muscle cell lines devoid of the drawbacks associated with the preparations of primary cultures of human myoblasts employed in D3 (cf page 2, lines 7-19 of the application).

The solution to the problem posed consists in the treatment of primary cultures of human myoblasts (of the type prepared in D3) to obtain conditionally immortalized derivatives thereof. To serve this purpose at least two different approaches are proposed, namely the use of (i) the temperature sensitive tsA58 variant of the large T-antigen or (II) the E1a-estrogen receptor chimera.

Although the conditionally immortalized human muscle cell lines thus prepared are expected to possess advantageous properties which overcome the aforementioned drawbacks (cf page 8, lines 17-24 of the application), no experimental support can be found elsewhere in the description as originally filed showing that such expected technical effects are obtained.

From the information provided in Example 1 it can be concluded that, in comparison with the results obtainable when using the rat L6 cell line (seemingly a currently available immortalized rodent cell line) the study of certain characteristics of the insulin mediated pathways of interest is facilitated by the use of the selected conditionally immortalized myogenic cell line of mouse origin hereby denominated C10. Nevertheless, these results do not necessarily substantiate an unexpected effect when bearing in mind the inferior performance of the glucose uptake system of the rat L6 cell line *versus* the mouse C2C12 cell line already disclosed in D2 (cf page 540, right column, last paragraph).

The technical information presented in Examples 2, 3 and 4 does not go beyond the teachings of the closest prior art D3, and therefore does not demonstrate that a solution to the problem posed has been provided.

With respect to Example 2, it is noted that on page 12, lines 29-31 the application states that *the cell lines produced have the added advantage of not having being subject to the diabetic milieu which can itself contribute to the insulin resistance seen at the cellular level* (i.e. the conditionally immortalized human myoblasts). However, the primary cultures of human myoblasts prepared in D3 also possessed said alleged advantage, since they were obtained from healthy subjects with no family history of diabetes (see page 872, left column, last paragraph, first sentence).

Moreover, neither Example 3 nor Example 4 provide the actual technical data corresponding to the respectively intended "Study of insulin action in immortalized human muscle cell lines" and "Use of human cell lines in an assay". In particular, no experimental results are provided showing any improved performance in the case of the conditionally immortalized myoblasts over the myotubes employed in D3 with respect to any of the comparative experiments supposedly carried out (e.g. the assay of kinases, assay of GS or glycogen synthesis).

Consequently, the application fails to contain the necessary technical information on the basis of which it could be possible to assess whether the various aspects of the alleged invention, particularly as defined in Claims 2, 3-6 (insofar as dependent on Claim 2) 7 and 8, involve an inventive step, contrary to the requirements of Art. 33(3) PCT.

## **SECTION VII**

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D2 is not mentioned in the description, nor are these documents identified therein.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/GB00/02674

2. The terms "Triton " (page 14, line 25), " Mono Q" (page 15, line 7), and "Sepharose" (page 15, line 16) appear to be registered trade marks, but have not been acknowledged as such.
3. The expression "hereby incorporated by reference" in respect of prior art documents on page 4, line 30 and page 18, lines 15-16 leads to a doubt as to whether the requirements of the description being self-contained are satisfied (see PCT Guidelines C-II, 4-17).

**SECTION VIII**

1. The statement in the description on page 18, lines 16-23 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (see also the PCT Guidelines, III-4.3a).
2. The embodiment of the invention described on page 6, lines 16-17 does not fall within the scope of the claims. This inconsistency between the claims and the description leads to doubt concerning the matter for which protection is sought, thereby rendering the claims unclear (Article 6 PCT).
3. The following expressions appear to contain clerical mistakes:  
  
"theraputic" (page 1, line 18)  
"prescence" (page 5, lines 8 and 9)  
"abscence" (page 5, lines 8 and 9)

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

HARDING, Charles Thomas  
D. YOUNG & CO.  
21 New Fetter Lane  
London EC4A 1DA  
GRANDE BRETAGNE

MONEY	£	11
ORDER		
DIARY		
REC'D	12 OCT 2001	
ANSO		
ENTRY		
FOR	ASA JPT	

# PCT

## NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing  
(day/month/year) 02.10.2001

Applicant's or agent's file reference  
P006824WO CTH

### IMPORTANT NOTIFICATION

International application No.  
PCT/GB00/02674

International filing date (day/month/year)  
11/07/2000

Priority date (day/month/year)  
13/07/1999

Applicant  
UNIVERSITY COLLEGE LONDON

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

#### 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

 European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized officer

Digiusto, M

Tel. +49 89 2399-8162

